DEPARTMENT OF HEALTH & HUMAN SERVICES

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February 28, 2001

Peder J. Estrup
Dean of Graduate School and Research
Brown University
Graduate School
Box 1867
Providence, PI 02912

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1411

Research Project: Learning Disabilities: Symptom Permanence and Consequences
Principal Investigator: Lewis Lipsitt
HHS Project Number: 5 R01 NS35208

Research Project: High-Risk Behaviors and the Prevalence of STD's among Women Prisoners at the Women's State Penitentiary in Metro Manila
Principal Investigator: Kenneth Mayer
HHS Project Number: 3 D43 TW00237

Dear Dr. Estrup:

The Office for Human Research Protections (OHRP) has reviewed your January 12, 2001 report concerning research involving prisoners as subjects that was conducted by Brown University (Brown).

Based upon its review, OHRP makes the following determinations:

(1) OHRP finds that the following corrective actions taken by Brown adequately address the findings made by OHRP in its November 27, 2000 letter:

(a) Brown has implemented policies and procedures regarding research involving prisoners. These include (i) having a prisoner or prisoner representative in attendance at any meeting in which such research is reviewed; (ii) requiring

investigators proposing such research to complete a checklist; (iii) documenting in the minutes of the Institutional Review Board (IRB) meetings that the findings required by Department of Health and Human Services (HHS) regulations at 45 CFR Part 46.305 have been made; and (iv) certifying approval to the Secretary of HHS for HHS-supported research.

(b) Brown's IRB Policies and Procedures have been modified to require submission of the grant application, to ensure continuing review of research at intervals appropriate to the degree of risk and not less than once per year, and to generally update the procedures.

(2) OHRP finds that Brown has adequately responded to the additional major concerns and questions raised by OHRP in its November 27, 2000 letter.

As a result of the above determinations, OHRP has closed its compliance oversight evaluation of the above-referenced research and anticipates no further OHRP involvement in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

At this time, OHRP provides the following additional recommendations and guidance.

(3) Regarding the research conducted under HHS Project Number 3 D43 TW00237, OHRP notes Brown's statement that the principal investigator confirmed that all informed consent information was presented to the research participants in their native language. The regulations require that informed consent information be presented "in language understandable to the subject" and, in most situations, that informed consent be documented in writing (see 45 CFR 46.116 and 46.117). Where informed consent is documented in accordance with HHS regulations at 45 CFR 46.117(b)(1), the written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent. Subjects who do not speak English should be presented with an informed consent document written in a language understandable to them. OHRP strongly encourages the use of this procedure whenever possible.

Alternatively, HHS regulations at 45 CFR 46.117(b)(2) permit oral presentation of informed consent information in conjunction with a short form written informed consent document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally, approved by the IRB and signed by the person obtaining consent. A witness to the oral presentation is required, who must sign the short form and the summary, and the subject must be given copies of the short form document and the summary. When this procedure is used with subjects who do not speak English, (i) the oral presentation and the short form written informed consent document should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be

fluent in both English and the language of the subject.
If research supported under 3 D43 TW00237 is ongoing and involves non-English-speaking subjects, the Brown IRB should ensure that informed consent is documented in accordance with the above guidance.

(4) OHRP acknowledges Brown's statement that a Single Project Assurance (SPA) was submitted to OHRP by the Philippine General Hospital for HHS project number 3 D43 TW00237, and that OHRP sent the SPA to this foreign site. However, OHRP received an incomplete SPA application from the Philippine General Hospital on February 16, 2001, and this SPA was never approved. If the above-mentioned project is ongoing, involvement of the Philippine General Hospital in human subject research activities under the above-referenced HHS award must be suspended until OHRP approves the assurance. Please consult with OHRP's Miss Freda Yonder (301-402-5793) for futher guidance regarding submission of an appropriate assurance.

(5) OHRP makes the following recommendations regarding the "Brown University Policies and Procedures for the Protection of Human Participants in Research:"

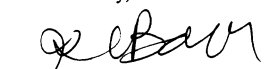
(a) Page 3 under "Equitable selection of research participants" discusses equitability and coercion. OHRP suggests that this section also discuss the need to minimize "undue influence."

(b) Page 5, last paragraph under "Protocol modifications" notes that approval letters regarding non-substantive changes will be sent to the investigator and recorded in the IRB files. OHRP notes that it may be appropriate to advise the IRB of approval of such changes at a full board meeting.

(c) Page 21, under "Reporting of unanticipated adverse events and death" does not note that unanticipated problems involving risks to subjects or others must be reported promptly to OHRP, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5). This section should be revised accordingly.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me if you have any questions.

Sincerely,



Kristina C. Borror, Ph.D.
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